

Message

From: Schlosser, Paul [Schlosser.Paul@epa.gov]
Sent: 12/20/2013 2:08:05 PM
To: Vulimiri, Suryanarayana [Vulimiri.Sury@epa.gov]; Subramaniam, Ravi [Subramaniam.Ravi@epa.gov]
CC: Glenn, Barbara [Glenn.Barbara@epa.gov]; Sonawane, Bob [Sonawane.Bob@epa.gov]; Bussard, David [Bussard.David@epa.gov]; White, Paul [White.Paul@epa.gov]; Kraft, Andrew [Kraft.Andrew@epa.gov]
Subject: RE: Formaldehyde Toxicokinetics

Heck et al. had collected tissues separately from what they called the "high tumor region" and "low tumor region" - both being respiratory (and transitional) epithelium. Thus these were sub-portions of the entire respiratory epithelium, and the Georgieva et al. model was parameterized rather carefully to match those sub-regions. Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP) That's a lot more work than I'd rather try to take on for this little analysis. And they could well have taken less than the whole thing and described it the same way.

-Paul

From: Vulimiri, Suryanarayana
Sent: Thursday, December 19, 2013 5:24 PM
To: Schlosser, Paul; Subramaniam, Ravi
Cc: Glenn, Barbara; Sonawane, Bob; Bussard, David; White, Paul; Kraft, Andrew
Subject: RE: Formaldehyde Toxicokinetics

Hi Paul,

Here is the information from the three studies of adduct analysis. The description is very general in the methods part for both Lu et al 2010 and Lu et al 2011.

Lu et al., 2010 – Fischer Rats 10 ppm HCHO 10 ppm for 1 or 5 days; 6 hrs/day

Nasal respiratory epithelium from the right and left sides of the nose and from the septum was collected, as were entire tissues of spleen, thymus, lung, and liver. Bone marrow was collected from both femurs by saline extrusion with a large bore needle. Tissue samples were collected and immediately frozen on dry ice followed by storage at -80oC.

Lu et al., 2011 – Fischer Rats 0.7, 2, 5.8, 9.1, or 15.2 ppm for 6 hrs
(They did not specify the region)

Briefly, rats were exposed to [13CD2]-formaldehyde for 6 h and sacrificed within 2 h following exposure. DNA was isolated from the nasal respiratory epithelium, followed by incubation with NaCNBH3 for 6 h to convert N2-hydroxymethyl-dG to stable N2-methyl-dG.

Moeller et al 2011 – Monkeys 1.9 and 6.1 ppm 6 hrs a day for 2 consecutive days
The nasal mucosa from maxilloturbinates and bone marrow were collected

Hope this information will be useful.
Sury

From: Schlosser, Paul
Sent: Thursday, December 19, 2013 3:59 PM
To: Subramaniam, Ravi
Cc: Glenn, Barbara; Sonawane, Bob; Bussard, David; White, Paul; Kraft, Andrew; Vulimiri, Suryanarayana
Subject: RE: Formaldehyde Toxicokinetics

I'm trying to do something quick here.

Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

I think this is good enough.

-Paul

From: Subramaniam, Ravi

Sent: Thursday, December 19, 2013 2:13 PM

To: Schlosser, Paul

Cc: Glenn, Barbara; Sonawane, Bob; Bussard, David; White, Paul; Kraft, Andrew; Vulimiri, Suryanarayana

Subject: RE: Formaldehyde Toxicokinetics

Paul

I have not looked at what you have here but thought I would bring this up.

Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

Ravi.

From: Schlosser, Paul

Sent: Thursday, December 19, 2013 1:59 PM

To: Kraft, Andrew; Vulimiri, Suryanarayana

Cc: Glenn, Barbara; Sonawane, Bob; Bussard, David; White, Paul; Subramaniam, Ravi

Subject: RE: Formaldehyde Toxicokinetics

Below is what I have right now. There's some modeling involved that will have to go into an appendix.

Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

From: Kraft, Andrew
Sent: Thursday, December 19, 2013 1:44 PM
To: Schlosser, Paul; Vulimiri, Suryanarayana
Cc: Glenn, Barbara; Sonawane, Bob; Bussard, David; White, Paul; Subramaniam, Ravi
Subject: RE: Formaldehyde Toxicokinetics

Thank you, Paul. I figured that was the case. Best of luck with the workshop planning, and thank you for continuing to think about this.

From: Schlosser, Paul
Sent: Thursday, December 19, 2013 1:43 PM
To: Kraft, Andrew; Vulimiri, Suryanarayana
Cc: Glenn, Barbara; Sonawane, Bob; Bussard, David; White, Paul; Subramaniam, Ravi
Subject: RE: Formaldehyde Toxicokinetics

I have been working on something, but the mouse lung tumor workshop is now taking precedence. It comes up Jan. 7-8. I will try to finish it shortly after that.

-Paul

From: Kraft, Andrew
Sent: Thursday, December 19, 2013 1:41 PM
To: Vulimiri, Suryanarayana
Cc: Glenn, Barbara; Sonawane, Bob; Bussard, David; Kraft, Andrew; White, Paul; Schlosser, Paul; Subramaniam, Ravi
Subject: Formaldehyde Toxicokinetics

Hi Sury,

As we had discussed, attached are the revision suggestions on the ADME section draft (which include an outline of the reorganization at the beginning). They include a revised organization, as well as a number of changes to the text (mostly aiming to highlight the uncertainties, and provide more fleshed out introductions/ conclusions). I know that the changes are substantial and it still needs a lot of work; I appreciate your willingness to take a close look and correct what needs correcting, and for filling in the blanks. I have also attached the version I worked from, in case you made changes after I started working on this revision.

I know that we were thinking Paul S. and Paul W. may also have some additions to the text regarding the methanediol and compartmentalization issues, respectively. As such, I have cc'd a bunch of people here who have expressed interested in this topic, and who have asked about an update to this section. Hopefully, this organization will help others to formulate their text ideas. If anybody has comments, suggestions, or corrections to this in-process draft, please share them with Sury, Barbara, and I. Please note that this point-of-first-contact organization is what we are really hoping to use in the end. Also, please don't share, but feel free to discuss. Thanks!

I will be on leave until next year, but I wanted to get this to you ASAP, Sury. We can discuss any questions you have (or may receive from others) when I return. Thanks again. I hope that you and your family have had/ continue to have a safe and wonderful holiday season.

Happy holidays to everyone else as well!

-Andrew